SUPPORTING INFORMATION

Ring-Closing Metathesis of Olefinic Peptides: Design, Synthesis, and Structural Characterization of Macrocyclic Helical Peptides

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General X-ray Crystallographic Data for Cyclic Peptide 8. Clear, colorless crystals of cyclic peptide **8** were obtained by slow diffusion from CH_2Cl_2/hexane at room temperature (20-25°C). The dimensions of the crystal analyzed were: 0.3 x 0.5 x 0.5 mm. The crystals belong to the orthorhombic system with unit cell parameters at 156 K: a = 19.30(1) Å, b = 24.73(2) Å, c = 12.134(7) Å, and V = 5791(6) $Å^3$. The space group is $P2_12_12_1$ with Z = 4 formula units/unit cell and ρ (calcd) = 1.246 g/cm^3. Intensity data (4698 total) was collected on a Picker (Crystal Logic) diffractometer system using monchromatized MoK_α radiation (λ = 0.7107 Å) *via* an θ-2θ

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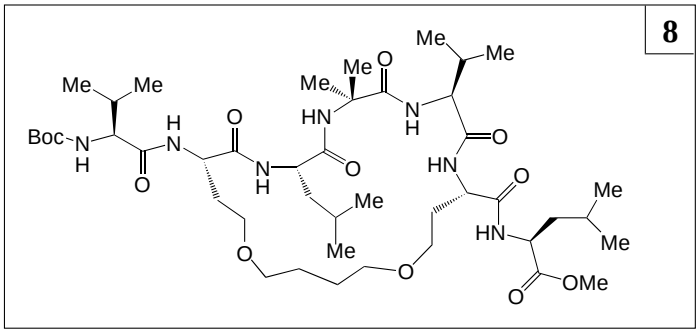
scan technique. Those 2266 reflections with $|I_o| > 3\sigma(|I_o|)$ were considered observed. An absorption correction was not applied.

The structure was solved by Direct Methods using the UCLA Crystallographic Computing Package[1] and SHELXTL 86 program set,[2] and refined by full-matrix least-squares techniques. There are two molecules of CH_2Cl_2 and one molecule of H_2O present per one peptide molecule. Hydrogen atoms were included using a riding model with d(C-H) = 0.96 Å and U(iso) = 0.08 Å2. At convergence, R_F = 6.6%, R_{wF} = 7.7% and *GOF* = 2.28 for 633 variables.



Crystallographic data (excluding structure factors) for structure **8** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101810. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Table S1. Details of X-ray data collection and structure refinement for cyclic peptide **8**.

Formula	C46 H85 Cl4 N7 O13
fw	1086.03
cryst syst	orthorhombic
space group	P212121
cryst color	colorless
cryst habit	irregular
a, Å	19.30(1)
b, Å	24.73(2)
c, Å	12.134(7)
Z	4
V, $Å^3$	5791(6)
ρ(calcd), g cm^{-3}	1.246
radiation, λ	Mo k_α .7107
abs coeff(μ), mm^{-1}	0.263
F(000), e	2328
temp, K	156
diffractometer	Picker (Crystal Logic)
scan mode, speed(deg/min)	θ-2θ, 6.0
2θ range, deg	1.6 - 50.0
total data collcd, unique data used	4698, 2266(I> 3σ(I))
no. of parms refined	633
final shift/error, max and avg	0.070, 0.004
max resid density, e/$Å^3$	0.80
$R = \Sigma\|\|F_o\|-\|F_c\|\|/\Sigma\|F_o\|$	0.066
$R_w = (\Sigma w(\|F_o\|-\|F_c\|)^2/\Sigma w(\|F_o\|)^2)^{1/2}$	0.077

Table S2. Distances, angles and torsion angles for the solid-state structure of cyclic peptide **8**.

O1	C4	1.41(2)	O1	C5	1.31(2)	O2	C5	1.26(2)
O3	C10	1.25(2)	O4	C12	1.241(16)	O5	C18	1.25(2)
O6	C22	1.22(2)	O7	C27	1.23(2)	O8	C29	1.24(2)
O9	C35	1.21(2)	O10	C35	1.35(2)	O10	C36	1.46(2)
O11	C38	1.46(2)	O11	C39	1.43(2)	O12	C42	1.40(2)
O12	C43	1.44(2)	N1	C5	1.35(2)	N1	C6	1.47(2)
N2	C10	1.34(2)	N2	C11	1.46(2)	N3	C12	1.31(2)
N3	C13	1.536(16)	N4	C18	1.35(2)	N4	C19	1.50(2)
N5	C22	1.37(2)	N5	C23	1.41(2)	N6	C27	1.34(2)
N6	C28	1.47(2)	N7	C29	1.37(2)	N7	C30	1.46(2)
C1	C4	1.53(2)	C2	C4	1.54(3)	C3	C4	1.50(3)
C6	C7	1.55(2)	C6	C10	1.51(2)	C7	C8	1.51(2)
C7	C9	1.53(2)	C11	C12	1.53(2)	C11	C44	1.57(2)
C13	C14	1.55(2)	C13	C18	1.46(2)	C14	C15	1.48(2)
C15	C16	1.55(2)	C15	C17	1.54(2)	C19	C20	1.54(2)
C19	C21	1.54(2)	C19	C22	1.58(2)	C23	C24	1.52(2)
C23	C27	1.56(2)	C24	C25	1.53(2)	C24	C26	1.57(2)
C28	C29	1.50(2)	C28	C37	1.52(2)	C30	C31	1.58(2)
C30	C35	1.49(2)	C31	C32	1.52(2)	C32	C33	1.53(2)
C32	C34	1.53(2)	C37	C38	1.52(2)	C39	C40	1.51(2)
C40	C41	1.52(2)	C41	C42	1.49(2)	C43	C44	1.51(2)

C4	O1	C5	121.5(13)	C35	O10	C36	115.1(12)
C38	O11	C39	111.0(10)	C42	O12	C43	113.0(10)
C5	N1	C6	123.3(12)	C10	N2	C11	118.7(11)
C12	N3	C13	115.7(11)	C18	N4	C19	122.9(11)
C22	N5	C23	119.2(11)	C27	N6	C28	121.9(11)
C29	N7	C30	119.6(11)	O1	C4	C1	104.7(13)
O1	C4	C2	111.4(14)	O1	C4	C3	112.8(14)
C1	C4	C2	106.5(15)	C1	C4	C3	111.9(15)
C2	C4	C3	109.3(15)	O1	C5	O2	127.3(15)
O1	C5	N1	112.9(14)	O2	C5	N1	119.7(14)
N1	C6	C7	109.0(11)	N1	C6	C10	111.8(12)
C7	C6	C10	114.2(12)	C6	C7	C8	112.4(11)
C6	C7	C9	112.4(12)	C8	C7	C9	108.5(12)
O3	C10	N2	122.9(13)	O3	C10	C6	120.2(13)
N2	C10	C6	116.6(13)	N2	C11	C12	112.5(11)
N2	C11	C44	108.7(11)	C12	C11	C44	112.9(11)
O4	C12	N3	124.2(12)	O4	C12	C11	118.5(12)
N3	C12	C11	117.1(12)	N3	C13	C14	106.3(10)
N3	C13	C18	111.1(11)	C14	C13	C18	113.8(11)
C13	C14	C15	113.4(11)	C14	C15	C16	111.3(12)
C14	C15	C17	111.7(12)	C16	C15	C17	108.3(12)
O5	C18	N4	119.7(13)	O5	C18	C13	121.5(12)
N4	C18	C13	118.7(12)	N4	C19	C20	109.8(12)
N4	C19	C21	110.7(11)	N4	C19	C22	110.1(11)
C20	C19	C21	110.3(12)	C20	C19	C22	106.0(12)
C21	C19	C22	109.9(12)	O6	C22	N5	125.8(13)
O6	C22	C19	119.2(13)	N5	C22	C19	115.0(12)
N5	C23	C24	108.9(11)	N5	C23	C27	113.4(11)
C24	C23	C27	110.5(11)	C23	C24	C25	109.4(11)
C23	C24	C26	111.2(11)	C25	C24	C26	109.8(11)
O7	C27	N6	123.0(13)	O7	C27	C23	123.0(12)
N6	C27	C23	113.9(12)	N6	C28	C29	113.7(11)

Table S2. Distances, angles and torsion angles for the solid-state structure of cyclic peptide **8** (cont.)

N6	C28	C37	109.3(10)	C29	C28	C37	109.1(11)
O8	C29	N7	122.1(13)	O8	C29	C28	120.7(12)
N7	C29	C28	117.2(12)	N7	C30	C31	110.7(11)
N7	C30	C35	111.3(12)	C31	C30	C35	108.8(12)
C30	C31	C32	112.3(11)	C31	C32	C33	108.8(11)
C31	C32	C34	112.3(12)	C33	C32	C34	110.9(12)
O9	C35	O10	122.5(15)	O9	C35	C30	127.4(15)
O10	C35	C30	110.0(13)	C28	C37	C38	113.0(11)
O11	C38	C37	108.5(11)	O11	C39	C40	108.3(12)
C39	C40	C41	115.4(12)	C40	C41	C42	114.9(12)
O12	C42	C41	110.7(11)	O12	C43	C44	108.6(11)
C11	C44	C43	115.3(12)				

C4	O1	C5	O2	4(2)	C4	O1	C5	N1	-172.6(14)
C38	O11	C39	C40	172.3(12)	C42	O12	C43	C44	-175.5(12)
C5	N1	C6	C7	-179.4(14)	C5	N1	C6	C10	-52(2)
C10	N2	C11	C12	-55.9(17)	C10	N2	C11	C44	178.3(13)
C12	N3	C13	C14	176.7(12)	C12	N3	C13	C18	-59.1(15)
C18	N4	C19	C20	-171.7(13)	C18	N4	C19	C21	66(2)
C18	N4	C19	C22	-55(2)	C22	N5	C23	C24	171.4(12)
C22	N5	C23	C27	-65.2(16)	C27	N6	C28	C29	-84.6(16)
C27	N6	C28	C37	153.2(13)	C29	N7	C30	C31	129.8(13)
C29	N7	C30	C35	-109.0(15)	C5	O1	C4	C1	-176.0(15)
C5	O1	C4	C2	-61(2)	C5	O1	C4	C3	62(2)
O1	C5	N1	C6	-180.0(13)	O2	C5	N1	C6	3(2)
N1	C6	C7	C8	-70.5(15)	N1	C6	C7	C9	166.8(12)
N1	C6	C10	O3	145.4(14)	N1	C6	C10	N2	-40(2)
C7	C6	C10	O3	-90(2)	C7	C6	C10	N2	84.4(16)
C10	C6	C7	C8	163.7(13)	C10	C6	C7	C9	41(2)
O3	C10	N2	C11	1(2)	C11	N2	C10	C6	-173.9(13)
N2	C11	C12	O4	156.3(12)	N2	C11	C12	N3	-28(2)
N2	C11	C44	C43	71.2(15)	C12	C11	C44	C43	-54.4(17)
O4	C12	N3	C13	-2(2)	O4	C12	C11	C44	-80.2(16)
C13	N3	C12	C11	-178.3(11)	N3	C12	C11	C44	95.9(15)
N3	C13	C14	C15	176.1(11)	N3	C13	C18	O5	145.5(13)
N3	C13	C18	N4	-37(2)	C14	C13	C18	O5	-94.7(16)
C14	C13	C18	N4	83.2(16)	C18	C13	C14	C15	53.6(16)
C13	C14	C15	C16	-177.9(12)	C13	C14	C15	C17	60.9(16)
O5	C18	N4	C19	-2(2)	C19	N4	C18	C13	-179.9(13)
N4	C19	C22	O6	146.7(13)	N4	C19	C22	N5	-35.9(17)
C20	C19	C22	O6	-94.6(16)	C20	C19	C22	N5	82.7(16)
C21	C19	C22	O6	24(2)	C21	C19	C22	N5	-158.2(13)
O6	C22	N5	C23	-1(2)	C23	N5	C22	C19	-178.3(12)
N5	C23	C24	C25	-62.2(14)	N5	C23	C24	C26	176.3(11)
N5	C23	C27	O7	154.8(13)	N5	C23	C27	N6	-30(2)
C24	C23	C27	O7	-83(2)	C24	C23	C27	N6	92.7(15)
C27	C23	C24	C25	172.6(12)	C27	C23	C24	C26	51.1(15)
O7	C27	N6	C28	5(2)	C28	N6	C27	C23	-170.2(12)
N6	C28	C29	O8	166.9(12)	N6	C28	C29	N7	-15(2)
N6	C28	C37	C38	-62.1(15)	C29	C28	C37	C38	173.0(12)
O8	C29	N7	C30	11(2)	O8	C29	C28	C37	-70.8(16)
C30	N7	C29	C28	-167.0(12)	N7	C29	C28	C37	107.1(14)
N7	C30	C31	C32	-60.6(15)	N7	C30	C35	O9	-11(2)
N7	C30	C35	O10	165.3(12)	C31	C30	C35	O9	111(2)

Table S2. Distances, angles and torsion angles for the solid-state structure of cyclic peptide **8** (cont.)

C31	C30	C35	O10	-72.4(15)	C35	C30	C31	C32	176.8(13)
C30	C31	C32	C33	-177.7(12)	C30	C31	C32	C34	-54.5(16)
O9	C35	O10	C36	-3(2)	C36	O10	C35	C30	-179.5(13)
C28	C37	C38	O11	173.2(11)	C39	O11	C38	C37	-178.3(12)
O11	C39	C40	C41	-67.2(16)	C39	C40	C41	C42	-85.1(16)
C40	C41	C42	O12	62.0(16)	C43	O12	C42	C41	-179.3(12)
O12	C43	C44	C11	75.0(15)					

Note: Units of distances are Angstroms, of angles degrees
E.s.d. in parentheses, in units of least significant digit
of the corresponding value

Table S3. Position and displacement parameters for the solid-state structure of cyclic peptide **8.**

Atom	x	y	z	U11 or <u Sq>	U22	U33	U12	U13	U23	Equiv <u Squared>
O1	0.1915(5)	0.4750(4)	0.7831(10)	0.035(6)	0.035(7)	0.103(10)	-0.021(5)	0.031(7)	-0.023(7)	0.058
O2	0.1876(5)	0.3821(4)	0.7930(8)	0.041(6)	0.044(7)	0.061(8)	0.021(5)	0.000(6)	-0.015(6)	0.049
O3	0.0516(5)	0.2982(4)	0.8664(8)	0.060(7)	0.025(6)	0.060(8)	0.013(5)	0.007(6)	0.007(6)	0.048
O4	0.0373(4)	0.2398(4)	0.5991(7)	0.030(6)	0.038(6)	0.044(7)	0.002(5)	0.000(5)	-0.009(5)	0.037
O5	0.1727(4)	0.1557(4)	0.6479(7)	0.043(6)	0.034(6)	0.032(6)	-0.003(5)	-0.002(5)	-0.016(5)	0.037
O6	0.0775(5)	0.0740(4)	0.8301(8)	0.073(8)	0.027(6)	0.060(8)	0.010(6)	-0.014(7)	0.004(6)	0.053
O7	0.0353(5)	0.0372(4)	0.5887(9)	0.046(6)	0.022(6)	0.086(9)	-0.019(5)	0.027(6)	-0.004(6)	0.051
O8	0.1387(5)	-0.0079(4)	0.4052(8)	0.069(8)	0.037(6)	0.037(7)	-0.007(6)	-0.003(6)	-0.008(6)	0.048
O9	0.1289(6)	-0.0727(4)	0.7158(9)	0.060(8)	0.057(7)	0.054(8)	0.016(7)	-0.009(7)	0.025(6)	0.057
O10	0.2315(6)	-0.1065(4)	0.6632(9)	0.073(8)	0.044(7)	0.058(8)	0.003(6)	0.012(7)	0.003(6)	0.058
O11	0.1112(5)	0.1988(4)	0.2972(8)	0.059(7)	0.033(6)	0.036(6)	0.010(6)	0.008(6)	0.007(5)	0.043
O12	0.0750(5)	0.3413(3)	0.4293(8)	0.035(6)	0.030(6)	0.041(6)	-0.008(5)	0.003(5)	-0.003(5)	0.035
N1	0.1091(7)	0.4349(4)	0.8802(10)	0.055(8)	0.040(8)	0.048(9)	0.013(7)	0.010(8)	-0.007(7)	0.048
N2	0.0314(5)	0.3662(4)	0.7439(10)	0.031(7)	0.030(7)	0.038(8)	-0.006(6)	-0.002(7)	-0.006(7)	0.033
N3	0.1245(6)	0.2954(4)	0.6501(9)	0.029(7)	0.023(6)	0.040(8)	0.009(6)	0.001(6)	-0.012(6)	0.031
N4	0.1438(6)	0.2079(4)	0.7923(10)	0.055(9)	0.020(6)	0.034(8)	0.003(6)	-0.008(7)	-0.003(7)	0.036
N5	0.0230(6)	0.1482(4)	0.7558(10)	0.031(7)	0.027(7)	0.044(8)	0.003(6)	-0.008(7)	0.007(6)	0.034
N6	0.0510(6)	0.0971(4)	0.5604(10)	0.026(7)	0.047(8)	0.035(8)	-0.012(6)	0.002(6)	0.006(7)	0.036
N7	0.1503(6)	0.0186(5)	0.5845(9)	0.037(8)	0.057(8)	0.016(7)	0.000(7)	-0.007(6)	-0.002(6)	0.037
C1	0.2631(9)	0.5375(7)	0.6960(20)	0.062(13)	0.069(14)	0.170(22)	-0.044(11)	0.047(15)	-0.028(14)	0.100
C2	0.3119(9)	0.4494(10)	0.7508(18)	0.045(12)	0.225(27)	0.093(17)	-0.003(16)	0.006(13)	0.005(19)	0.121
C3	0.2271(9)	0.4528(7)	0.5971(16)	0.079(14)	0.054(12)	0.084(15)	-0.010(11)	0.024(13)	0.009(11)	0.072
C4	0.2460(9)	0.4773(6)	0.7062(15)	0.034(10)	0.058(12)	0.070(13)	0.004(9)	0.019(11)	-0.012(11)	0.054
C5	0.1662(8)	0.4289(7)	0.8169(14)	0.027(10)	0.067(13)	0.049(12)	0.009(10)	0.005(9)	-0.011(11)	0.048
C6	0.0709(7)	0.3889(6)	0.9283(12)	0.048(10)	0.038(10)	0.043(11)	-0.001(8)	0.005(9)	-0.017(9)	0.043
C7	0.0084(7)	0.4109(5)	0.9944(12)	0.045(10)	0.032(8)	0.030(10)	0.002(8)	0.005(8)	0.005(7)	0.035
C8	0.0302(7)	0.4395(6)	1.0988(12)	0.047(10)	0.045(9)	0.043(11)	0.015(8)	0.000(9)	-0.004(9)	0.045
C9	-0.0432(8)	0.3664(7)	1.0248(13)	0.062(11)	0.076(12)	0.045(12)	0.030(11)	0.018(10)	0.016(10)	0.061
C10	0.0522(7)	0.3472(6)	0.8423(14)	0.032(9)	0.033(10)	0.049(12)	0.005(8)	0.015(9)	-0.006(9)	0.038
C11	0.0061(7)	0.3278(5)	0.6618(13)	0.025(8)	0.034(8)	0.050(11)	0.003(7)	-0.001(8)	-0.005(8)	0.036
C12	0.0587(7)	0.2835(5)	0.6365(11)	0.031(9)	0.026(8)	0.035(10)	-0.006(7)	0.005(8)	0.001(8)	0.030
C13	0.1761(7)	0.2503(5)	0.6206(12)	0.036(9)	0.015(8)	0.045(10)	0.007(7)	0.005(8)	0.005(8)	0.032
C14	0.2493(7)	0.2747(5)	0.6362(12)	0.016(8)	0.040(9)	0.051(11)	-0.003(7)	0.006(8)	0.000(8)	0.036
C15	0.3059(7)	0.2351(6)	0.6183(13)	0.027(9)	0.049(10)	0.049(11)	-0.004(8)	0.004(9)	-0.014(9)	0.042
C16	0.3777(8)	0.2609(7)	0.6390(13)	0.054(11)	0.081(12)	0.064(13)	-0.004(10)	-0.010(11)	-0.038(11)	0.066
C17	0.3049(7)	0.2123(6)	0.5003(15)	0.035(9)	0.058(11)	0.078(13)	0.011(9)	0.001(9)	-0.018(11)	0.057
C18	0.1636(7)	0.2020(6)	0.6864(12)	0.034(9)	0.039(10)	0.024(10)	-0.007(8)	-0.006(8)	-0.016(8)	0.032
C19	0.1299(8)	0.1609(6)	0.8669(12)	0.058(11)	0.040(9)	0.034(11)	0.018(9)	-0.001(9)	0.009(9)	0.044
C20	0.0983(10)	0.1811(6)	0.9757(13)	0.111(16)	0.055(11)	0.031(11)	0.024(11)	-0.005(11)	-0.002(8)	0.066
C21	0.1969(8)	0.1290(6)	0.8895(13)	0.069(11)	0.039(9)	0.050(11)	0.017(9)	-0.023(10)	0.004(9)	0.053
C22	0.0739(8)	0.1225(6)	0.8138(12)	0.043(10)	0.045(11)	0.028(10)	-0.011(9)	0.002(9)	-0.003(8)	0.038
C23	-0.0304(7)	0.1174(5)	0.7077(12)	0.018(8)	0.037(8)	0.035(10)	0.014(7)	0.009(7)	0.015(8)	0.030
C24	-0.0859(7)	0.1556(6)	0.6637(12)	0.021(8)	0.048(10)	0.050(11)	0.004(8)	0.019(8)	0.013(9)	0.040
C25	-0.1169(8)	0.1878(6)	0.7592(14)	0.055(10)	0.037(9)	0.059(12)	0.012(8)	0.016(10)	0.015(9)	0.051
C26	-0.1447(7)	0.1237(6)	0.6021(14)	0.030(9)	0.046(10)	0.094(14)	-0.001(8)	0.004(10)	0.026(10)	0.056

Table S3. Position and displacement parameters for the solid-state structure of cyclic peptide **8** (cont.)

Atom	x	y	z	U11 or <u Sq>	U22	U33	U12	U13	U23	Equiv <u Squared>
C27	-0.0047(8)	0.0787(5)	0.6147(12)	0.037(10)	0.030(9)	0.036(10)	0.010(8)	-0.014(9)	0.015(8)	0.034
C28	0.0764(6)	0.0709(5)	0.4593(11)	0.027(8)	0.031(9)	0.023(9)	-0.005(7)	0.007(7)	0.004(7)	0.027
C29	0.1235(7)	0.0237(5)	0.4803(12)	0.052(10)	0.018(9)	0.034(11)	-0.024(8)	0.015(9)	0.000(8)	0.035
C30	0.2071(7)	-0.0190(6)	0.6041(12)	0.028(9)	0.047(10)	0.038(10)	0.007(8)	0.012(9)	0.012(8)	0.038
C31	0.2679(7)	0.0097(5)	0.6686(11)	0.038(9)	0.033(9)	0.034(10)	0.014(8)	-0.005(8)	0.007(7)	0.035
C32	0.2978(7)	0.0572(6)	0.6056(12)	0.023(8)	0.049(10)	0.033(10)	-0.008(8)	-0.003(8)	0.006(8)	0.035
C33	0.3582(8)	0.0810(6)	0.6717(13)	0.052(11)	0.057(11)	0.052(12)	0.000(9)	0.008(10)	0.021(9)	0.054
C34	0.3211(8)	0.0414(6)	0.4893(14)	0.052(11)	0.046(10)	0.065(13)	-0.017(9)	0.009(10)	0.001(9)	0.054
C35	0.1836(9)	-0.0669(6)	0.6687(14)	0.042(11)	0.042(11)	0.048(12)	-0.022(9)	0.002(10)	0.004(9)	0.044
C36	0.2139(10)	-0.1560(6)	0.7230(14)	0.120(17)	0.015(8)	0.079(14)	-0.018(9)	-0.006(13)	0.014(10)	0.071
C37	0.1144(7)	0.1123(5)	0.3892(12)	0.048(10)	0.028(8)	0.040(10)	-0.009(8)	-0.002(9)	-0.001(8)	0.039
C38	0.0683(7)	0.1584(6)	0.3518(12)	0.051(10)	0.050(10)	0.037(10)	0.011(9)	0.016(9)	0.005(9)	0.046
C39	0.0705(8)	0.2442(6)	0.2628(13)	0.049(10)	0.053(10)	0.048(11)	-0.004(9)	-0.007(9)	-0.002(9)	0.050
C40	0.1191(8)	0.2877(6)	0.2214(12)	0.047(10)	0.052(11)	0.043(11)	-0.002(9)	0.000(9)	0.013(9)	0.047
C41	0.1654(7)	0.3134(5)	0.3087(12)	0.035(9)	0.042(9)	0.035(10)	-0.010(7)	-0.007(8)	0.008(8)	0.037
C42	0.1332(8)	0.3591(5)	0.3709(12)	0.054(10)	0.027(9)	0.044(10)	-0.007(8)	-0.005(9)	0.004(8)	0.041
C43	0.0413(7)	0.3841(6)	0.4900(13)	0.035(9)	0.039(9)	0.060(12)	-0.006(9)	-0.003(9)	0.008(9)	0.045
C44	-0.0168(7)	0.3509(6)	0.5568(13)	0.038(9)	0.054(10)	0.047(10)	0.006(8)	-0.008(9)	-0.007(9)	0.046
OIW	0.5062(7)	0.5262(4)	0.1928(9)	0.175(13)	0.043(7)	0.050(8)	0.046(8)	0.016(9)	0.008(6)	0.089
CL1	0.503(1)	0.465(1)	0.827(1)	0.07(1) *						
CL1A	0.526(1)	0.447(1)	0.841(2)	0.06(1) *						
CL1B	0.467(5)	0.483(4)	0.842(8)	0.23(1) *						
CL2	0.420(1)	0.417(1)	0.999(1)	0.13(1) *						
CL2A	0.440(2)	0.370(1)	0.920(3)	0.08(1) *						
CL2B	0.413(1)	0.463(1)	1.013(2)	0.04(1) *						
CL2C	0.435(1)	0.389(1)	0.972(2)	0.04(1) *						
C1S	0.483(1)	0.459(1)	0.964(2)	0.10(1) *						
CL3	0.749(1)	0.137(1)	0.958(1)	0.05(1) *						
CL3A	0.754(2)	0.198(1)	1.027(3)	0.24(1) *						
CL3B	0.745(1)	0.177(1)	0.959(2)	0.07(1) *						
CL4	0.867(1)	0.238(1)	1.053(2)	0.20(1) *						
CL4A	0.789(1)	0.238(1)	0.998(2)	0.12(1) *						
CL4B	0.819(1)	0.244(1)	1.033(2)	0.06(1) *						
C2S	0.814(2)	0.169(2)	1.083(4)	0.29(1) *						
H1A	0.313	0.547	0.686	0.08 *						
H1B	0.243	0.559	0.758	0.08 *						
H1C	0.237	0.547	0.627	0.08 *						
H2A	0.314	0.413	0.715	0.09 *						
H2B	0.309	0.444	0.832	0.09 *						
H2C	0.356	0.469	0.733	0.09 *						
H3A	0.175	0.453	0.593	0.06 *						
H3B	0.245	0.415	0.590	0.06 *						
H3C	0.246	0.475	0.536	0.06 *						
H6	0.101	0.370	0.982	0.04 *						
H7	-0.014	0.437	0.941	0.04 *						

Table S3. Position and displacement parameters for the solid-state structure of cyclic peptide **8** (cont.)

Atom	x	y	z	<u Sq>	
H8A	0.072	0.461	1.080	0.05	*
H8B	0.044	0.409	1.149	0.05	*
H8C	-0.006	0.462	1.134	0.05	*
H9A	-0.031	0.332	0.986	0.06	*
H9B	-0.092	0.377	1.007	0.06	*
H9C	-0.039	0.360	1.106	0.06	*
H11	-0.032	0.307	0.698	0.04	*
H13	0.172	0.240	0.541	0.03	*
H14A	0.253	0.287	0.715	0.04	*
H14B	0.256	0.307	0.587	0.04	*
H15	0.302	0.202	0.666	0.06	*
H16A	0.386	0.289	0.581	0.06	*
H16B	0.417	0.234	0.640	0.06	*
H16C	0.374	0.279	0.713	0.06	*
H17A	0.336	0.180	0.493	0.06	*
H17B	0.321	0.242	0.450	0.06	*
H17C	0.256	0.202	0.482	0.06	*
H20A	0.086	0.149	1.024	0.07	*
H20B	0.056	0.204	0.966	0.07	*
H20C	0.135	0.203	1.013	0.07	*
H21A	0.235	0.153	0.919	0.05	*
H21B	0.213	0.111	0.821	0.05	*
H21C	0.185	0.101	0.946	0.05	*
H23	0.052	0.094	0.767	0.04	*
H24	-0.059	0.179	0.611	0.03	*
H25A	-0.133	0.164	0.820	0.06	*
H25B	-0.157	0.210	0.731	0.06	*
H25C	-0.081	0.213	0.789	0.06	*
H26A	-0.123	0.116	0.529	0.06	*
H26B	-0.185	0.148	0.590	0.06	*
H26C	-0.161	0.089	0.634	0.06	*
H28	0.037	0.055	0.417	0.03	*
H30	0.222	-0.028	0.527	0.04	*
H31A	0.305	-0.018	0.680	0.04	*
H31B	0.249	0.022	0.742	0.04	*
H32A	0.264	0.087	0.592	0.04	*
H33A	0.366	0.120	0.660	0.04	*
H33B	0.402	0.061	0.659	0.04	*
H33C	0.343	0.075	0.749	0.04	*
H34A	0.362	0.018	0.505	0.05	*
H34B	0.337	0.077	0.459	0.05	*
H34C	0.286	0.023	0.440	0.05	*
H36A	0.257	-0.174	0.752	0.06	*
H36B	0.189	-0.182	0.674	0.06	*
H36C	0.183	-0.146	0.786	0.06	*

Table S3. Position and displacement parameters for the solid-state structure of cyclic peptide **8** (cont.)

Atom	x	y	z	<u Sq>	
H37A	0.135	0.094	0.323	0.04	*
H37B	0.152	0.129	0.434	0.04	*
H38A	0.034	0.144	0.297	0.04	*
H38B	0.043	0.175	0.415	0.04	*
H39A	0.042	0.258	0.325	0.04	*
H39B	0.039	0.233	0.201	0.04	*
H40A	0.094	0.318	0.186	0.05	*
H40B	0.150	0.270	0.166	0.05	*
H41A	0.210	0.326	0.276	0.04	*
H41B	0.175	0.285	0.365	0.04	*
H42A	0.168	0.379	0.417	0.04	*
H42B	0.115	0.384	0.313	0.04	*
H43A	0.019	0.409	0.437	0.06	*
H43B	0.075	0.405	0.537	0.06	*
H44A	-0.048	0.390	0.582	0.04	*
H44B	-0.043	0.334	0.508	0.04	*
H1N	0.093	0.466	0.916	0.04	*
H2N	0.034	0.406	0.727	0.04	*
H3N	0.137	0.333	0.688	0.04	*
H4N	0.126	0.237	0.828	0.04	*
H5N	0.038	0.184	0.754	0.04	*
H6N	0.085	0.128	0.581	0.04	*
H7N	0.141	0.046	0.649	0.04	*

DISPLACEMENT PARAMETERS ARE COMMONLY CALLED VIBRATION PARAMETERS
UNITS OF U(I,J) AND ISOTROPIC <u Squared> ARE ANGSTROMS SQUARED
UNITS OF EACH E.S.D., IN PARENTHESES, ARE THOSE OF THE
LEAST SIGNIFICANT DIGIT OF THE CORRESPONDING PARAMETER
ISOTROPIC VALUES ARE [1/(8 PI-SQUARED)] TIMES THE "EQUIVALENT
B VALUE" DEFINED BY W. C. HAMILTON (1959) ACTA CRYST. 12, 609-610
"ANISOTROPIC TEMPERATURE FACTOR" DEFINED AS:
EXP[-2.0x(PI SQUARED)x(U11xA*xA*xHxH + U22xB*xB*xKxK + U33xC*xC*xLxL + 2.0xU12xA*xB*xHxK
+ 2.0xU13xA*xC*xHxL + 2.0xU23xB*xC*xKxL)]
* DENOTES AN ATOM REFINED ISOTROPICALLY, HYDROGEN ATOMS WERE CALCULATED AND NOT REFINED.

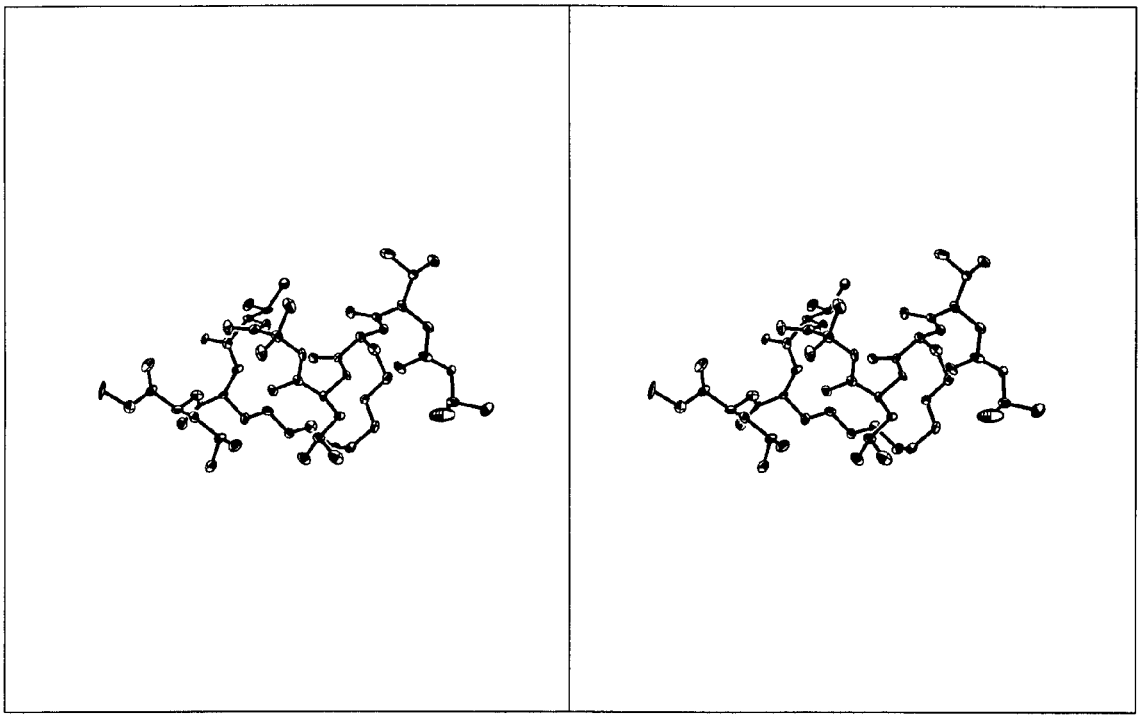


Figure S1. stereoview of ORTEP diagram for cyclic peptide **8**.

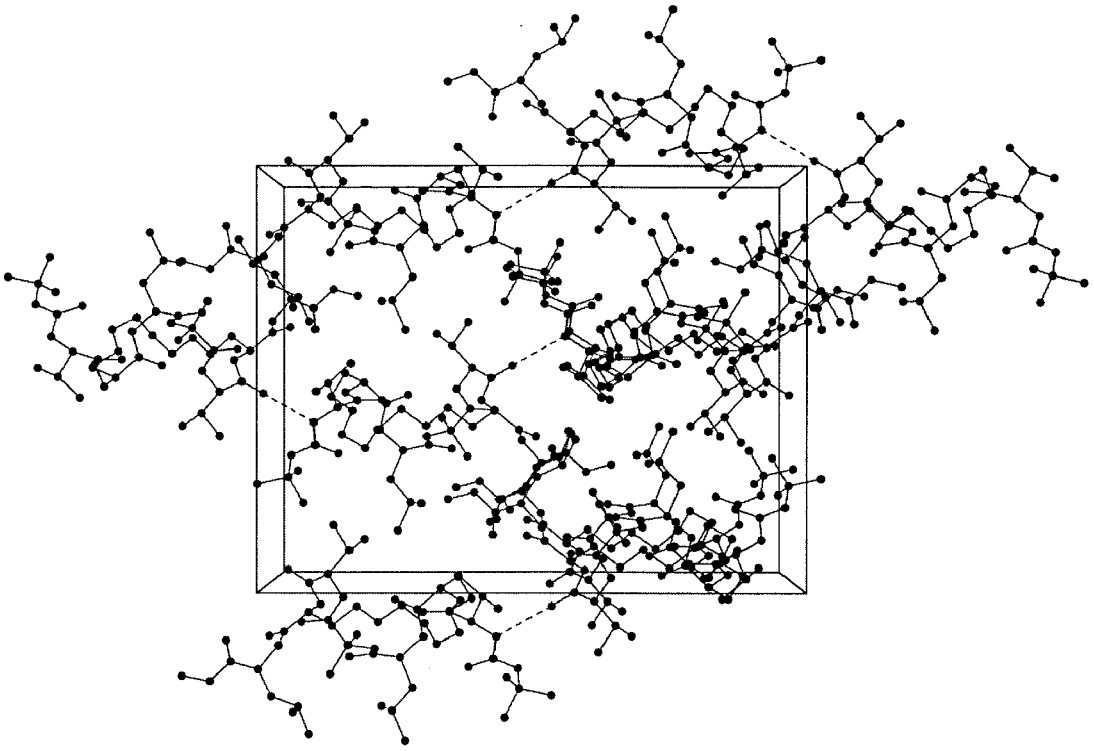


Figure S2. Unit cell of cyclic peptide **8**.

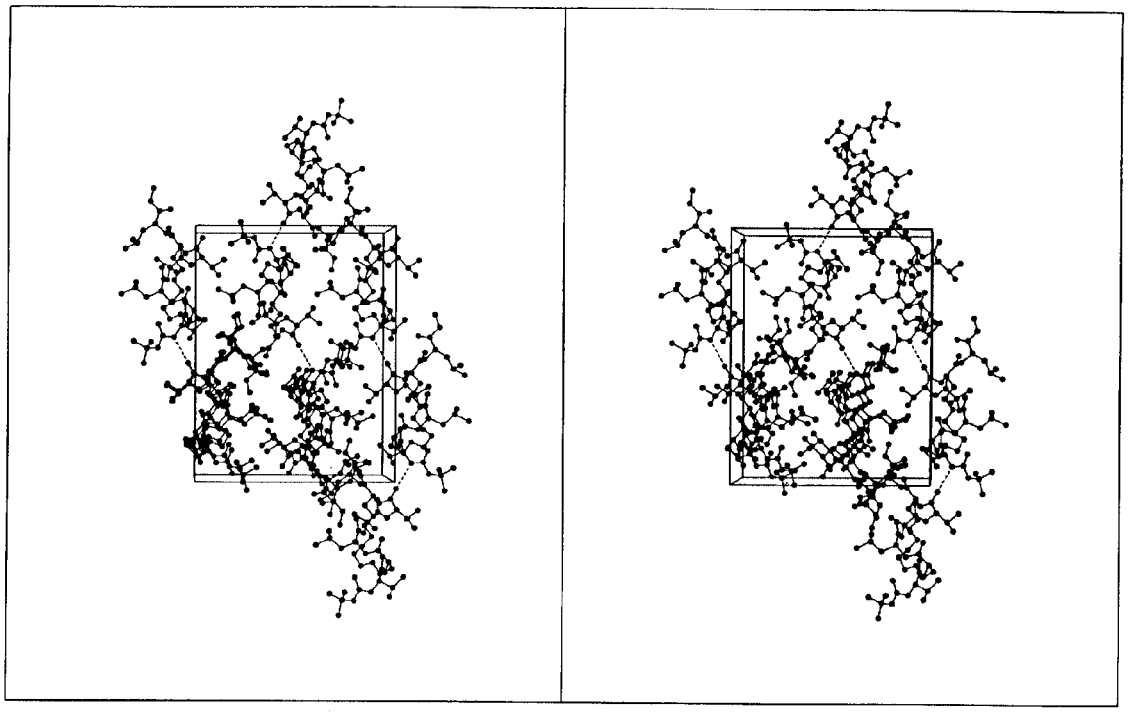


Figure S3. Stereoview of unit cell of cyclic peptide **8**.

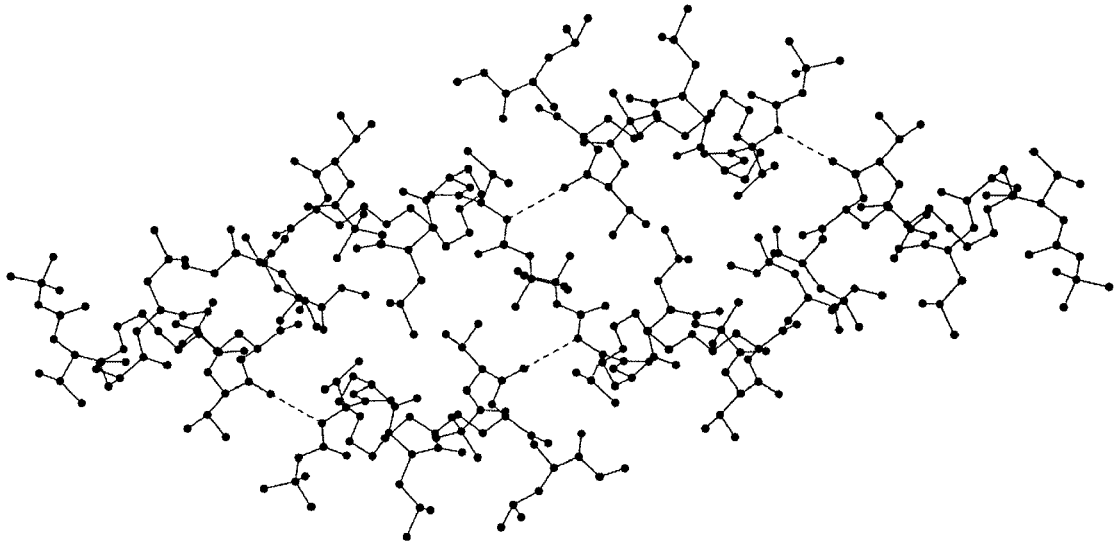


Figure S4. Six molecules from the unit cell of cyclic peptide **8**.

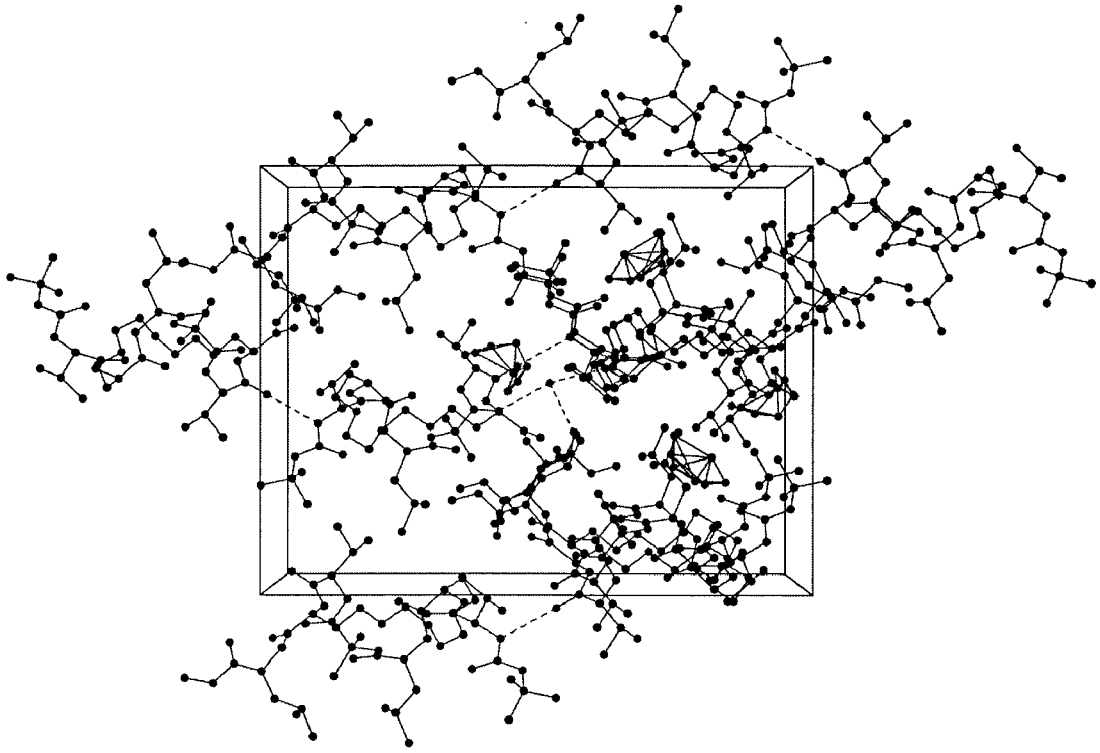


Figure S5. Unit cell of cyclic peptide **8** including solvent molecules.

Table S4. ^{1}H NMR data for acyclic peptide **4** (30 mM, CD_2Cl_2, 25 °C). All atoms are labeled moving out from the α carbon in the order: α, β, γ, δ, ε, ζ, and η. In cases of magnetic inequivalence of diastereotopic protons, the higher field proton was arbitrarily labeled with a prime (') symbol because stereospecific assignments were not made.

Residue	Proton	δ (ppm)
BOC	CH_3	1.48
Val1	NH ($J_{NH\alpha}$ = 2.0 Hz)	5.03
	αH ($J_{\alpha\beta}$ = 4.4 Hz)	3.75
	βH	2.12
	γH	1.02
	γ'H	0.99
Hse2	NH ($J_{NH\alpha}$ = 3.4 Hz)	8.11
	αH ($J_{\alpha\beta1}$ = 4.4 Hz, $J_{\alpha\beta2}$ = 8.3 Hz)	4.19
	βH	2.14
	β'H	1.96
	γH	3.65
	γ'H	3.50
	εH	3.99
	ζH	5.95
	η_{cis}H	5.25
	η_{trans}H	5.32
Leu3	NH ($J_{NH\alpha}$ = 6.4 Hz)	7.37
	αH (overlap with Val5αH)	4.47
	βH, β'H	~1.7
	γH	~1.7
	δH	0.95
	δ'H	0.88
Aib4	NH	7.61
	βCH_3	1.50
	β'CH_3	1.46
Val5	NH ($J_{NH\alpha}$ = 6.4 Hz)	6.89
	αH ($J_{\alpha\beta}$ = 4.4 Hz)	4.08
	βH	2.40
	γH, γ'H	1.01
Hse6	NH ($J_{NH\alpha}$ = 8.1 Hz)	7.55
	αH ($J_{\alpha\beta1}$ = 3.9 Hz, $J_{\alpha\beta2}$ = 11.3 Hz)	4.37
	βH	2.22
	β'H	1.96
	γH	3.52
	γ'H	3.50
	εH	3.91
	ζH	5.87
	η_{cis}H	5.09
	η_{trans}H	5.21
Leu7	NH ($J_{NH\alpha}$ = 8.1 Hz)	7.21
	αH ($J_{\alpha\beta1}$ = 5.5 Hz, $J_{\alpha\beta2}$ = 8.6 Hz)	4.47
	βH, β'H	~1.7
	γH	~1.7
	δH, δ'H	0.89
OMe	CH_3	3.68

Table S5. ^{1}H NMR data for cyclic peptide **8** (30 mM, CD_2Cl_2, 25 °C). All atoms are labeled moving out from the α carbon in the order: α, β, γ, δ, ε, ζ, and η. In cases of magnetic inequivalence of diastereotopic protons, the higher field proton was arbitrarily labeled with a prime (') symbol because stereospecific assignments were not made.

Residue	Proton	δ (ppm)
BOC	CH_3	1.49
Val1	NH ($J_{NH\alpha}$ = 2.0 Hz)	5.17
	αH ($J_{\alpha\beta}$ = 4.4 Hz)	3.82
	βH	2.16
	γH	1.04
	γ'H	0.99
Hse2	NH ($J_{NH\alpha}$ = 3.9 Hz)	6.76
	αH (overlap with Val5αH)	4.18
	βH	2.34
	β'H	1.77
	γH, γ'H	3.50
	εH	3.26
	ζH	1.35
Leu3	NH ($J_{NH\alpha}$ = 3.9 Hz)	7.24
	αH ($J_{\alpha\beta1}$ = 4.6 Hz, $J_{\alpha\beta2}$ = 7.8 Hz)	3.98
	βH, β'H	1.61
	γH	1.78
	δH	0.97
	δ'H	0.92
Aib4	NH	7.48
	βCH_3	1.68
	β'CH_3	1.47
Val5	NH ($J_{NH\alpha}$ = 7.8 Hz)	7.83
	αH ($J_{\alpha\beta}$ = 6.9 Hz)	4.18
	βH	2.45
	γH	1.07
	γ'H	1.00
Hse6	NH ($J_{NH\alpha}$ = 8.8 Hz)	7.55
	αH ($J_{\alpha\beta1}$ = 3.4 Hz, $J_{\alpha\beta2}$ = 11.5 Hz)	4.27
	βH, β'H	2.12
	γH	3.51
	γ'H	3.38
	εH	3.38
	ζH	1.52
Leu7	NH ($J_{NH\alpha}$ = 8.3 Hz)	7.05
	αH ($J_{\alpha\beta1}$ = 6.4 Hz, $J_{\alpha\beta2}$ = 8.5 Hz)	4.48
	βH, β'H	1.64
	γH	1.74
	δH	0.89
	δ'H	0.87
OMe	CH_3	3.69

Table S6. Interproton distance restraints for peptides **4** and **8** calculated by integration of the crosspeaks in Tr-ROESY spectra (CD_2Cl_2 (*c* = 30 mM), 25 °C, 2048 x 256 data matrix, 16 scans/FID, 600 msec composite spin-lock pulse).[3] Restraints added in the second refinement round of calculation are shaded in gray.

Acyclic Peptide **4** (32 restraints)		Cyclic Peptide **8** (35 restraints)	
Proton Pair	Restraint Upper-Bound (Å)	Proton Pair	Restraint Upper-Bound (Å)
Val1NH, Val1α	3	Val1NH, Val1α	3
Hse2NH, Hse2α	3	Leu3NH, Leu3α	3
Hse6NH, Hse6α	3	Hse6NH, Hse6α	3
Leu7NH, Leu7α	3	Leu7NH, Leu7α	3
Val5NH, Val5β	3	Val5NH, Val5β	3
Hse6α, Leu7NH	3	Val1α, Hse2NH	4
Val1NH, Hse2NH	3	Leu3α, Aib4NH	4
Hse2NH, Leu3NH	3	Hse6α, Leu7NH	3
Leu3NH, Aib4NH	3	Val1NH, Hse2NH	4
Aib4NH, Val5NH	3	Hse2NH, Leu3NH	4
Val5NH, Hse6NH	3	Leu3NH, Aib4NH	3
Hse6NH, Leu7NH	3	Aib4NH, Val5NH	3
Leu3NH, Leu3α	3	Val5NH, Hse6NH	3
Val5NH, Val5α	3	Hse6NH, Leu7NH	3
Hse2NH, Hse2ε	5	Val1α, Leu3NH	4
Val1α, Hse2NH	4	Leu3α, Hse6NH	4
Hse2α, Leu3NH	4	Val1α, Aib4NH	4
Leu3α, Aib4NH	4	Leu3α, Val5NH	4
Hse2β/β', Leu3NH	5	Hse2NH, Hse2α	3
Aib4β/β', Val5NH	5	Hse2α, Leu3NH	4
Val5β, Hse6NH	4	Val5α, Hse6NH	4
Hse6β/β', Leu7NH	5	Val5α, Aib4β/β'	5
Val1γ/γ', Hse2NH	5	Val1β, Hse2NH	4
Val5γ/γ', Hse6NH	7	Aib4β/β', Val5NH	5
Val1α, Leu3NH	4	Hse6β/β', Leu7NH	5
Hse2α, Aib4NH	4	Val1γ/γ', Hse2NH	7
Val5α, Leu7NH	4	Hse2γ/γ', Leu3NH	6
Aib4β/β', Hse6NH	6	Hse2α, Aib4NH	4
Val1α, Aib4NH	4	Leu3α, Hse6β/β'	5
Val1NH, BOC	8	Leu3α, Hse6ε	6
Hse2NH, BOC	8	Val1NH, BOC	8
Hse2ζ, BOC	8	Val1α, BOC	8
		Leu7α, OMe	5
		Hse2NH, BOC	8
		Leu3NH, BOC	8

Figure S6. Phi-Psi maps for all seven residues in refined conformations of acyclic peptide **4**. Data for ideal 3_{10}- and α-helices are also shown.

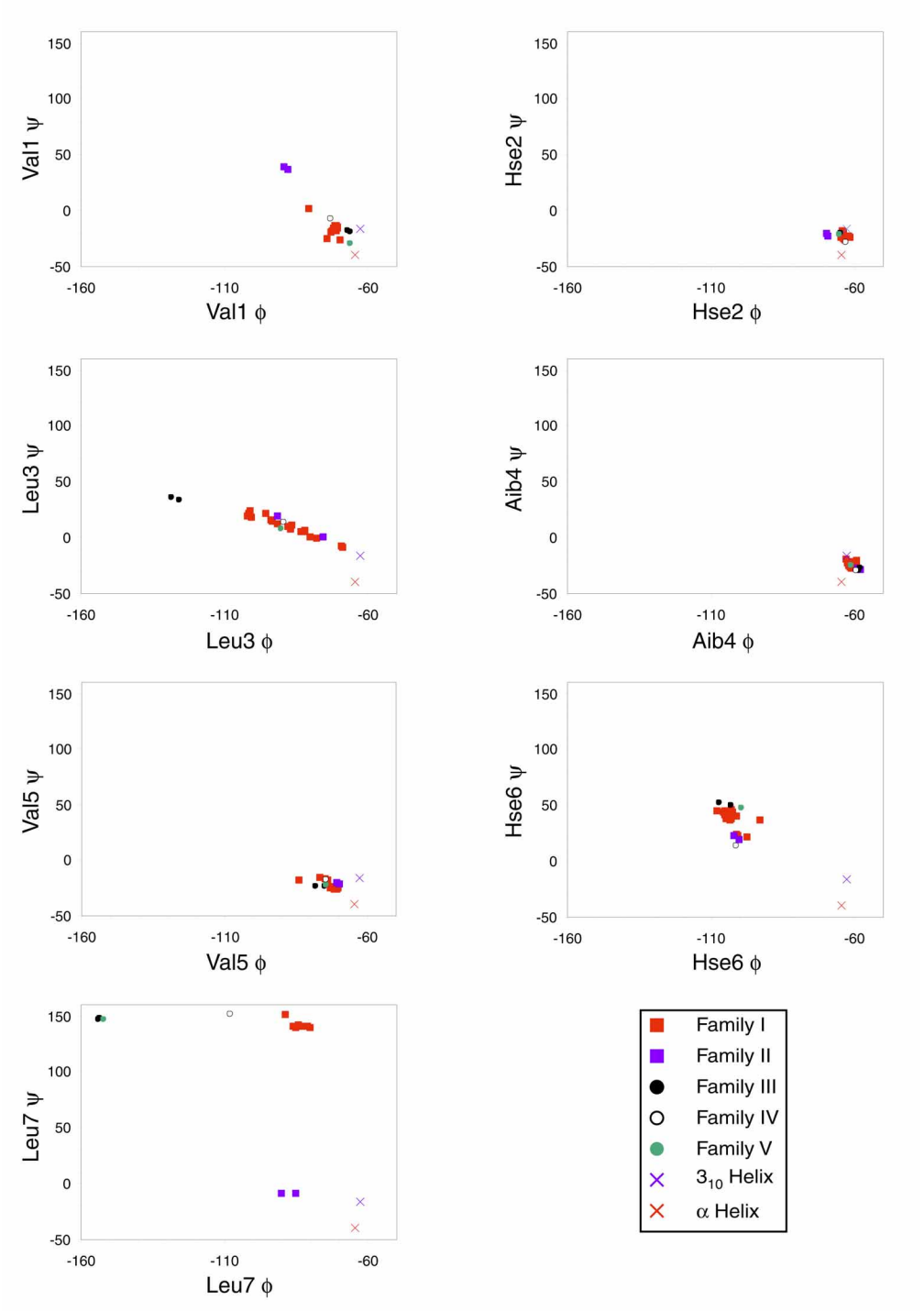


Figure S7. Phi-Psi maps for all seven residues in refined conformations of cyclic peptide **8**. Data for ideal 3_{10}- and α-helices are also shown. CH = cyclic peptide helix **8**.

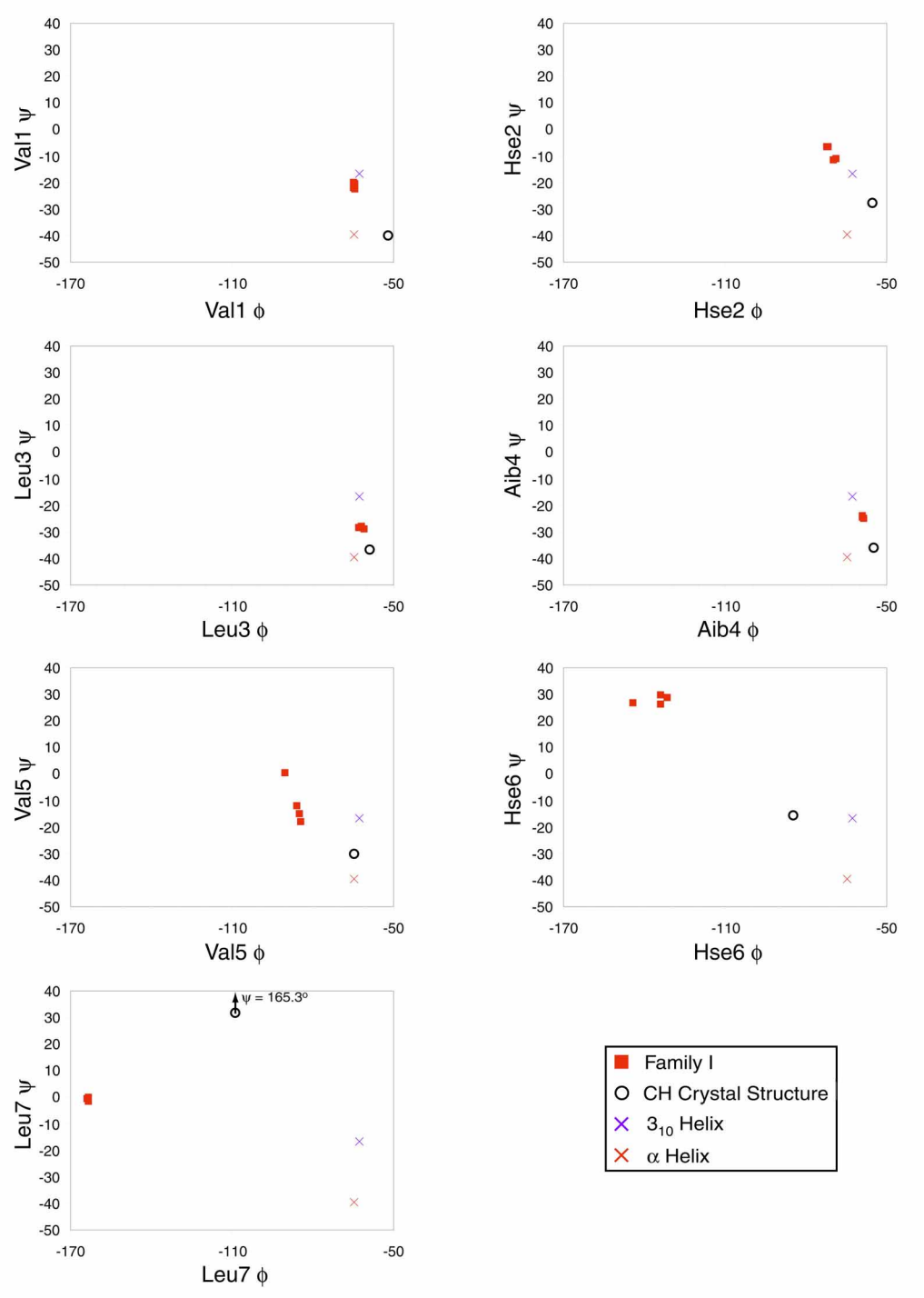


Figure S8. Rendered images of SYBYL .mol2 files for five calculated families (I-V) of conformers for acyclic peptide **4**.[4]

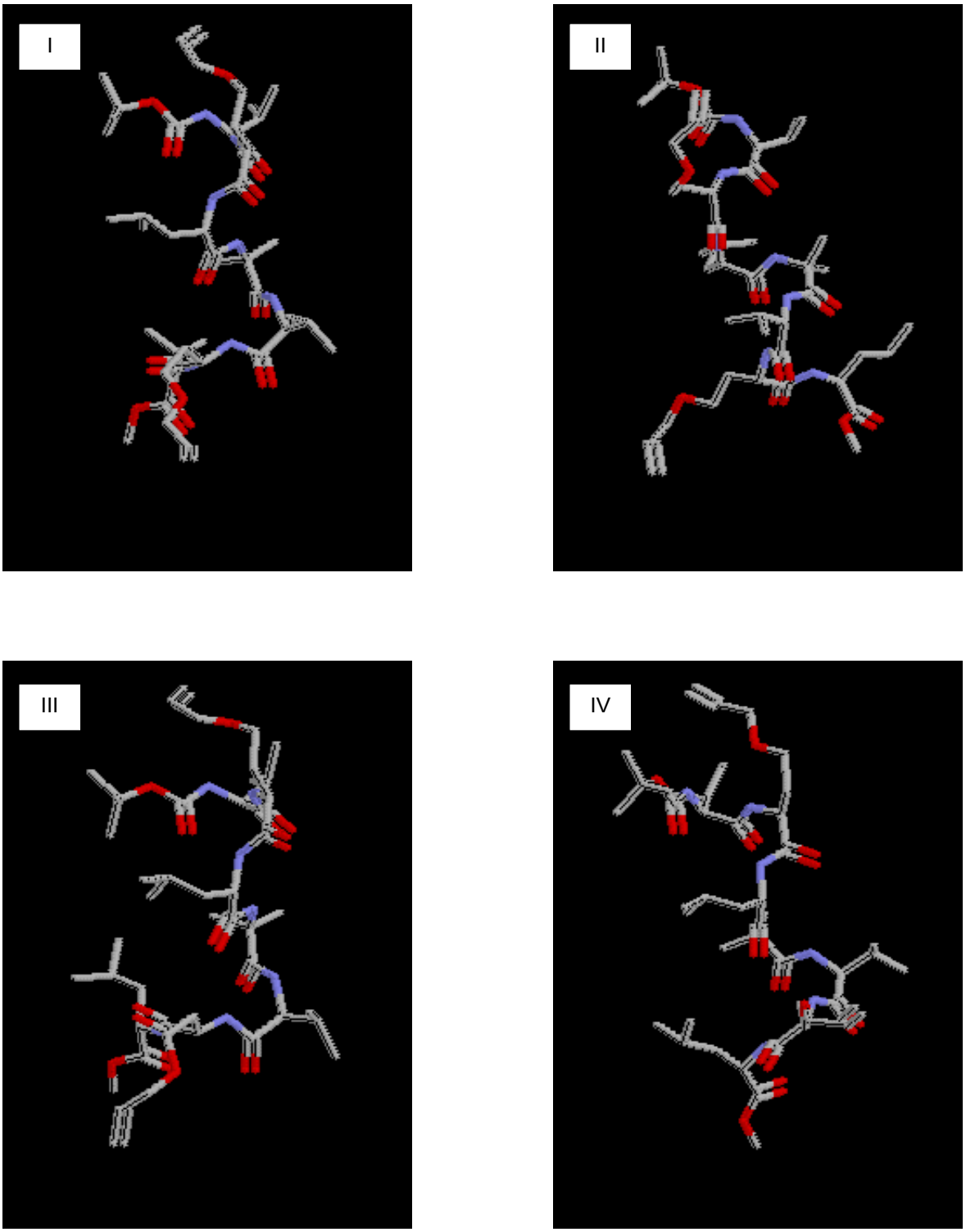


Figure S8. Rendered image of SYBYL .mol2 files for five calculated families (I-V) of conformers for acyclic peptide **4** (cont.)[4]

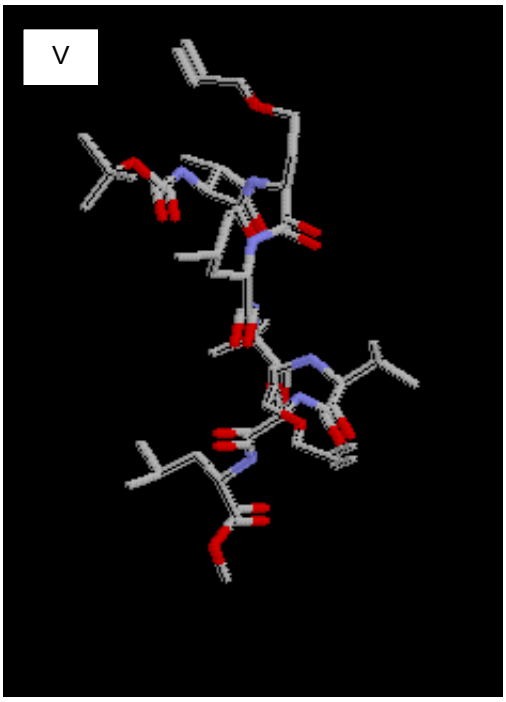
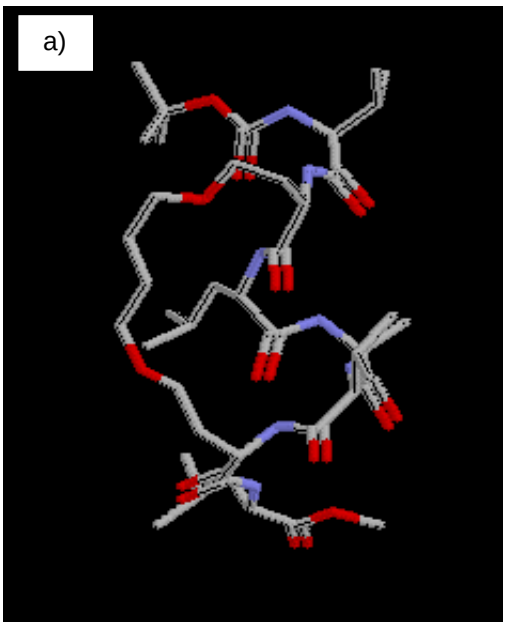
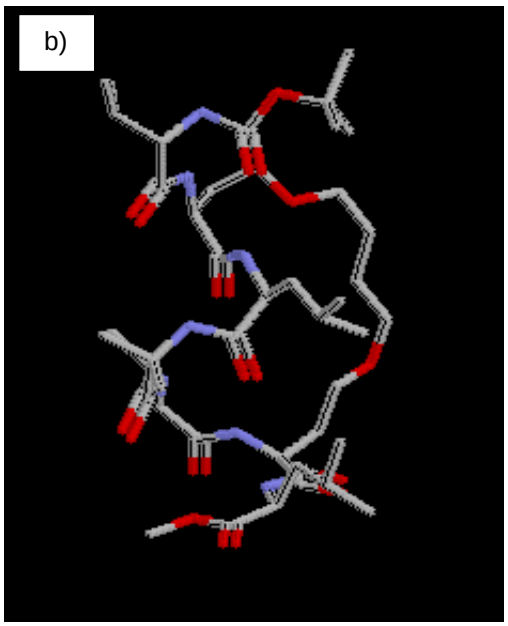


Figure S9. Two rendered images of SYBYL .mol2 files (a, b) for one calculated family of conformers for cyclic peptide **8**.[4]





References and Notes.

(1) UCLA Crystallographic Computing Package, University of California, Los Angeles, 1981.

(2) Sheldrick, G. M.; SHELXS-86 *Acta Crystallogr*. **1990**, *A46*, 467-473.

(3) Bax, A.; Davis, D. G. *J. Magn. Reson.* **1985**, *65*, 355-360.

(4) Restrained conformational searching were conducted for both heptapeptides **4** and **8** using the RandomSearch algorithm of SYBYL 6.6 (Tripos Software, St. Louis, MO). The RandomSearch algorithm for each run searched conformational space in two steps, repeated in sequence for 2000 total iterations: (step 1) random rotation of up to 3 torsional angles in the molecule, and (step 2) restrained energy minimization of the resulting structure using the static Merck Molecular Force-Field, MMFF94s. See: Halgren, T. *J. Comp. Chem.* **1999**, *20*, 720-729.